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## **CLAIMS**

- An automated method of optimising crystallisation conditions for macromolecules comprising the step of forming a crystallisation trial, the trial comprising a sample comprising (i) a gel forming component and (ii) the macromolecule to be crystallised, wherein at least one component of the trial is dispensed using an automatic liquid dispensing system.
- 10 2. A method according to Claim 1 wherein a layer of oil is present over the sample.
- A method according to Claim 2 wherein the sample and oil are dispensed from different tips of the automatic liquid dispensing system.
  - 4. A method according to Claims 2 or 3 wherein the oil is dispensed first and the sample is dispensed under the oil.
- 20 5. A method according to any one of Claims 1 to 4 wherein the surface onto which the gel-forming component or sample is dispensed is a greased surface.
- 6. A method according to Claim 5 wherein the grease is a high-vacuum silicone grease.
  - 7. A method according to Claim 1 further comprising the steps of
    - (i) incubating the sample as a drop in the presence of a first reservoir with a composition having a higher solute concentration that that of the sample; and

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- (ii) transferring the drop into the presence of a second reservoir with a composition having a lower solute concentration than the first reservoir by means of an automatic robot.
- 5 8. The method according to Claim 7 wherein the first reservoir composition is covered with a layer of oil.
  - 9. A method according to Claim 2 or 8 wherein the oil layer permits diffusion from the sample.
  - 10. The method according to any one of Claims 1 to 9 wherein the gelforming component is or comprises agarose or tetramethyl ortho silane (TMOS).
- 15 11. The method of Claim 10 wherein the gel-forming component is or comprises TMOS and is at a final concentration of 0.2%.
  - 12. The method of any one of Claims 1 to 11 wherein the volume of sample dispensed is less than 5µl.
  - 13. The method of Claim 12 wherein the volume of sample is between 1.5µl and 2µl.
- 14. The method of any one of Claims 1 to 13 wherein the oil layer includes paraffin.
  - 15. The method of any one of Claims 1 to 14 wherein the oil layer is a mixture of oils.
- 30 16. The method of Claim 15 wherein the oil layer comprises silicone.

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- 17. The method of any one of Claims I to 15 wherein the oil layer consists of paraffin.
- 5 18. The method of any one of Claims 1 to 17 wherein the sample is dispensed into wells of a 1536-well microassay plate.
  - 19. A method according to Claim 1 to 18 wherein the oil layer over the sample permits vapour diffusion between the sample and the environment due to the thinness of the layer.
  - 20. Use of an automated liquid dispensing system capable of dispensing volumes of liquid between 0.1µl to 5µl for dispensing a sample of gelforming component and a macromolecule to be crystallised.

21. Use of a gel-forming component in automated optimisation of crystallisation of macromolecules.

- Use according to Claim 20 or 21 wherein the optimisation includes a method according to any one of Claims 1 to 19.
  - 23. Use according to any one of Claims 20 to 22 wherein the gel-forming component is 0.2% TMOS.
- 25 24. Use of oil in a method according to any one of Claims 1 to 19.
  - 25. Use according to Claim 24 wherein the oil is a mixture of oils.
  - 26. Use according to Claim 25 wherein the mixture comprises silicone.

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- 27. Use according to any one of Claims 20 to 26 wherein the oil includes paraffin.
- 28. Use of a grease in a method according to any one of Claims 1 to 6.
- 29. Use according to Claim 28 wherein the grease is a high-vacuum silicon grease.
- 30. Use according to Claim 28 or 29 wherein the grease is provided on a multi-well plate.
  - 31. Use of an automated liquid dispensing system in a method according to any one of Claims 1 to 19.
- 15 32. Use according to Claim 31 wherein the automated liquid dispensing system is IMPAX or Oryx 6.
  - 33. A kit of parts comprising an automated liquid dispensing system and a gel-forming component.
  - 34. A kit according to Claim 33 wherein the gel-forming component is or comprises TMOS.
  - 35. A kit according to Claim 33 or 34 further comprising a low density oil.
  - 36. A kit of parts comprising an automated liquid dispensing system, low density oil and grease.
  - 37. A kit according to Claim 36 wherein the grease is a high-vacuum silicon grease.

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- 38. A kit according to Claim 36 or 37wherein the grease is provided on a multi-well plate.
- 5 39. A kit according to any one of Claims 35 to 38 wherein the oil is paraffin.
  - 40. A method, use or kit according to any one of the previous claims wherein the macromolecule is a biological macromolecule.
  - 41. A method, use or kit according to Claim 40 wherein the biological macromolecule is a polypeptide.